

IN THE CLAIMS:

Please substitute original claims numbered 1, 4, 5, 8, 23 and 34 with the following amended claims having the same claim numbers.

Please add new claims numbered 36-66 for consideration.

1. (currently amended) A therapeutic method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), ~~Alzheimer's disease (AD)~~, cerebrovascular dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of at least one agent capable of inhibiting a neuronal cell cycle progression.
2. (original) The therapeutic method of claim 1, wherein the at least one agent is capable of inhibiting neuronal cell cycle progression before entry of a neuronal cell into a synthesis (S) phase.
3. (original) The therapeutic method of claim 1, wherein the at least one agent is capable of inhibiting neuronal cell cycle progression at or prior to the early growth ( $G_1$ ) phase.
4. (currently amended) The therapeutic method of claim 1, wherein the at least one agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, sirolimus, any sirolimus derivative capable of inhibiting inhibiting early cell cycle progression, flavopiridol, ciclopirox, a paulone, indirubin, fascaplycin, olomoucine, roscovitine, Aragasterol A, valproate, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, a farnesyl transferase inhibitor such as R115777, SCH66336 and BMS-214662, and sodium butyrate.
5. (currently amended) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), ~~Alzheimer's disease (AD)~~, cerebrovascular

dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of (i) at least one first agent capable of inhibiting neuronal cell cycle division before entry of a neuronal cell into an early phase or of said cell cycle, and optionally (ii) at least one second agent capable of inhibiting cell cycle progression at any one or more of the phases of the cell cycle.

6. (original) The method of claim 5, wherein the at least one first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, sirolimus, any sirolimus derivative capable of inhibiting early cell cycle progression, a paulone, indirubin, fascaplycin, olomoucine, roscovitine, Aragasterol A, valproate, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, a farnesyl transferase inhibitor such as R115777, SCH66336 and BMS-214662, and sodium butyrate.

7. (original) The method of claim 5, wherein the at least one second agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate.

8. (currently amended) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), ~~Alzheimer's disease (AD)~~, cerebrovascular dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of:

- i) at least one first agent capable of inhibiting neuronal cell cycle progression at or before an early phase;
- ii) at least one second agent capable of inhibiting neuronal cell cycle progression generally; and optionally
- iii) at least one third agent capable of inhibiting mitogenic stimulation.

9. (original) The method of claim 8 wherein the first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell

cycle progression, sirolimus, any sirolimus derivative capable of inhibiting early cell cycle progression, a paulone, indirubin, fascaplycin, olomoucine, roscovitine, Aragasterol A, valproate, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, a farnesyl transferase inhibitor such as R115777, SCH66336 and BMS-214662, and sodium butyrate.

10. (original) The method of claim 8, wherein the second agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate.

11. (original) The method of claim 8 wherein the third agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.

12. (original) The method of claim 11, wherein the inhibitor of glutamate-induced excitotoxicity is selected from the group consisting of memantine, neramexane, amantadine, riluzole, MK801, ketamine, dextromethorphan, dextrorphan, phencyclidine, and dexanabinol (HU-211).

13. (original) The method of claim 11, wherein the inhibitor of activated microglia-induced mitogenic stimulation is an anti-inflammatory agent.

14. (original) The method of claim 13, wherein the anti-inflammatory agent is selected from the group consisting of non-steroidal anti-inflammatory agents (NSAIDS), salicylates, steroids, and immunophillins.

15. (original) The method of claim 14, wherein the NSAID is selected from the group consisting of ibuprofen, naproxen, celecoxib, rofecoxib, sulindac, piroxicam, indomethacin, etodolac, nabumetone, tolmetin, diclofenac, ketoprofen, apazone, and meloxicam.

16. (original) The method of claim 14, wherein the steroid is a glucocorticoid.

17. (original) The method of claim 16, wherein the glucocorticoid is prednisone.
18. (original) The method of claim 14, wherein the immunophillins is selected from the group consisting of cyclosporine A and tacrolimus.
19. (original) The method of claim 5, wherein the first agent is capable of inhibiting neuronal cell cycle progression at, or prior to entry into, the early growth ( $G_1$ ) phase.
20. (original) The method of claim 5, wherein the first agent is capable of inhibiting neuronal cell cycle progression at, or prior to entry into, the synthesis (S) phase.
21. (original) The method of claim 20, wherein the agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle response, sirolimus, any sirolimus derivative capable of inhibiting early cell cycle progression, a paulone, indirubin, fascaplycin, olomoucine, roscovitine, Aragasterol A, valproate, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, a farnesyl transferase inhibitor such as R115777, SCH66336 and BMS-214662, and sodium butyrate.
22. (original) The method of claim 1, wherein the subject is a human.
23. (currently amended) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), ~~Alzheimer's disease (AD)~~, or cerebrovascular dementia (CVD), in a subject with AAMI, MCI, ~~AD~~, or CVD, comprising administering a therapeutically effective amount of (i) at least one first agent capable of inhibiting neuronal cell cycle progression, and (ii) at least one second agent capable of reducing mitogenic stimulation.
24. (original) The method of claim 23, wherein the at least one first agent inhibits cell cycle progression prior to entry of a neuronal cell into a synthesis (S) phase and the at

least one second agent is capable of inhibiting glutamate-induce excitotoxicity and/or reducing activated microglia-induced mitogenic stimulation.

25. (original) The method of claim 23, wherein the at least one first agent inhibits cell cycle progression at or prior to entry of a neuronal cell into, an early growth ( $G_1$ ) phase and the at least one second agent is capable of inhibiting glutamate-induce excitotoxicity and/or reducing activated microglia-induced mitogenic stimulation.

26. (original) The therapeutic method of claim 23, wherein the at least one first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, sirolimus, any sirolimus derivative capable of inhibiting early cell cycle progression, a paulone, indirubin, fascaplycin, olomoucine, roscovitine, Aragusterol A, valproate, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, a farnesyl transferase inhibitor such as R115777, SCH66336 and BMS-214662, and sodium butyrate.

27. (original) The method of claim 23 wherein the second agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.

28. (original) The method of claim 27, wherein the inhibitor of glutamate-induced excitotoxicity is selected from the group consisting of memantine, neramexane, amantadine, riluzole, MK801, ketamine, dextromethorphan, dextrorphan, phencyclidine, and dexanabinol (HU-211).

29. (original) The method of claim 27, wherein the inhibitor of activated microglia-induced mitogenic stimulation is an anti-inflammatory agent.

30. (original) The method of claim 29, wherein the anti-inflammatory agent is selected from the group consisting of non-steroidal anti-inflammatory agents (NSAIDS), salicylates, steroids, and immunophillins.

31. (original) The method of claim 30, wherein the NSAID is selected from the group consisting of ibuprofen, naproxen, celecoxib, rofecoxib, sulindac, piroxicam, indomethacin, etodolac, nabumetone, tolmetin, diclofenac, ketoprofen, apazone, and meloxicam.
32. (original) The method of claim 30, wherein the steroid is a glucocorticoid.
33. (original) The method of claim 32, wherein the glucocorticoid is prednisone.
34. (currently amended) The method of claim 30, wherein the ~~immunophillins~~ immunophillin is selected from the group consisting of cyclosporine A and tacrolimus.
35. (original) The method of claim 23 wherein the at least one first agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate and the at least one second agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.
36. (new) A therapeutic method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), Alzheimer's disease (AD), cerebrovascular dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of at least one agent capable of inhibiting a neuronal cell cycle progression.
37. (new) The therapeutic method of claim 36, wherein the at least one agent is capable of inhibiting neuronal cell cycle progression before entry of a neuronal cell into a synthesis (S) phase.
38. (new) The therapeutic method of claim 36, wherein the at least one agent is capable of inhibiting neuronal cell cycle progression at or prior to the early growth ( $G_1$ ) phase.

39. (new) The therapeutic method of claim 36, wherein the at least one agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, flavopiridol, ciclopirox, a paulone, indirubin, olomoucine, roscovitine, Aragusterol A, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, and a farnesyl transferase inhibitor such as R115777, SCH66336 or BMS-214662.

40. (new) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), Alzheimer's disease (AD), cerebrovascular dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of (i) at least one first agent capable of inhibiting neuronal cell cycle division before entry of a neuronal cell into an early phase of said cell cycle, and optionally (ii) at least one second agent capable of inhibiting cell cycle progression at any one or more of the phases of the cell cycle.

41. (new) The method of claim 40, wherein the at least one first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, a paulone, indirubin, olomoucine, roscovitine, Aragusterol A, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, and a farnesyl transferase inhibitor such as R115777, SCH66336 or BMS-214662.

42. (new) The method of claim 40, wherein the at least one second agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate.

43. (new) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), Alzheimer's disease (AD), cerebrovascular dementia (CVD) and related retrogenic degenerative neurological conditions, comprising administering a therapeutically effective amount of:

i) at least one first agent capable of inhibiting neuronal cell cycle progression at or before an early phase;

- ii) at least one second agent capable of inhibiting neuronal cell cycle progression generally; and optionally
  - iii) at least one third agent capable of inhibiting mitogenic stimulation.

44. (new) The method of claim 43 wherein the first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, a paulone, indirubin, olomoucine, roscovitine, Aragusterol A, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, and a farnesyl transferase inhibitor such as R115777, SCH66336 or BMS-214662.

45. (new) The method of claim 43, wherein the second agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate.

46. (new) The method of claim 43 wherein the third agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.

47. (new) The method of claim 46, wherein the inhibitor of glutamate-induced excitotoxicity is selected from the group consisting of memantine, neramexane, amantadine, riluzole, MK801, ketamine, dextromethorphan, dextrorphan, phencyclidine, and dexanabinol (HU-211).

48. (new) The method of claim 46, wherein the inhibitor of activated microglia-induced mitogenic stimulation is an anti-inflammatory agent.

49. (new) The method of claim 48, wherein the anti-inflammatory agent is selected from the group consisting of non-steroidal anti-inflammatory agents (NSAIDS), salicylates, and immunophillins.

50. (new) The method of claim 49, wherein the NSAID is selected from the group consisting of ibuprofen, naproxen, celecoxib, rofecoxib, sulindac, piroxicam,

indomethacin, etodolac, nabumetone, tolmetin, diclofenac, ketoprofen, apazone, and meloxicam.

51. (new) The method of claim 49, wherein the immunophillin is cyclosporine A.

52. (new) The method of claim 40, wherein the first agent is capable of inhibiting neuronal cell cycle progression at, or prior to entry into, the early growth ( $G_1$ ) phase.

53. (new) The method of claim 40, wherein the first agent is capable of inhibiting neuronal cell cycle progression at, or prior to entry into, the synthesis (S) phase.

54. (new) The method of claim 53, wherein the agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle response, a paulone, indirubin, olomoucine, roscovitine, Aragasterol A, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, and a farnesyl transferase inhibitor such as R115777, SCH66336 or BMS-214662.

55. (new) The method of claim 36, wherein the subject is a human.

56. (new) A method of treating age associated memory impairment (AAMI), mild cognitive impairment (MCI), Alzheimer's disease (AD), or cerebrovascular dementia (CVD), in a subject with AAMI, MCI, AD, or CVD, comprising administering a therapeutically effective amount of (i) at least one first agent capable of inhibiting neuronal cell cycle progression, and (ii) at least one second agent capable of reducing mitogenic stimulation.

57. (new) The method of claim 56, wherein the at least one first agent inhibits cell cycle progression prior to entry of a neuronal cell into a synthesis (S) phase and the at least one second agent is capable of inhibiting glutamate induce excitotoxicity and/or reducing activated microglia-induced mitogenic stimulation.

58. (new) The method of claim 56, wherein the at least one first agent inhibits cell cycle progression at or prior to entry of a neuronal cell into, an early growth ( $G_1$ ) phase and the at least one second agent is capable of inhibiting glutamate-induce excitotoxicity and/or reducing activated microglia-induced mitogenic stimulation.

59. (new) The therapeutic method of claim 56, wherein the at least one first agent is selected from the group consisting of minocycline, any tetracycline family derivative capable of crossing the blood brain barrier, acetylsalicylic acid, any salicylate which inhibits early phase cell cycle progression, a paulone, indirubin, olomoucine, roscovitine, Aragusterol A, N-(3-chloro-7-indolyl)-1,4-benzenedisulfamide, and a farnesyl transferase inhibitor such as R115777, SCH66336 or BMS-214662.

60. (new) The method of claim 56 wherein the second agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.

61. (new) The method of claim 60, wherein the inhibitor of glutamate-induced excitotoxicity is selected from the group consisting of memantine, neramexane, amantadine, riluzole, MK801, ketamine, dextromethorphan, dextrorphan, phencyclidine, and dexanabinol (HU-211).

62. (new) The method of claim 60, wherein the inhibitor of activated microglia-induced mitogenic stimulation is an anti-inflammatory agent.

63. (new) The method of claim 62, wherein the anti-inflammatory agent is selected from the group consisting of non-steroidal anti-inflammatory agents (NSAIDS), salicylates, and immunophillins.

64. (new) The method of claim 62, wherein the NSAID is selected from the group consisting of ibuprofen, naproxen, celecoxib, rofecoxib, sulindac, piroxicam, indomethacin, etodolac, nabumetone, tolmetin, diclofenac, ketoprofen, apazone, and meloxicam.

65. (new) The method of claim 63, wherein the immunophillin is cyclosporine A.

66. (new) The method of claim 56 wherein the at least one first agent is selected from the group consisting of flavopiridol, ciclopirox, and methotrexate and the at least one second agent acts to inhibit glutamate-induced excitotoxicity and/or activated microglia-induced mitogenic stimulation.